



## Amphotericin B Induced Hyperbilirubinemia - A Rare Case Report

Mary Jacob<sup>1</sup>, Jeslyn Mary Philip<sup>1</sup>, Gireesh Kumar K. P<sup>2</sup>, Naveen Kumar Panicker\*<sup>3</sup>

<sup>1</sup>Pharm D Student, Dept of Pharmacy Practice, Amrita School of Pharmacy, AIMS Campus, Kochi, Amrita Vishwa Vidyapeetham, Amrita University, India.

<sup>2</sup>Department of Emergency Medicine, Amrita Institute of Medical Sciences, AIMS Campus, Kochi, India.

<sup>3</sup>Lecturer, Dept of Pharmacy Practice, Amrita School of Pharmacy, AIMS Campus, Kochi, Amrita Vishwa Vidyapeetham, Amrita University, India.

\*Corresponding author's E-mail: [naveenkumarpanicker@aims.amrita.edu](mailto:naveenkumarpanicker@aims.amrita.edu)

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### ABSTRACT

Hyperbilirubinemia is a state where there is increase of bilirubin in the blood. Bilirubin is brownish yellow in colour and is originated from bile. The liver breaks down the red blood cells that are old to generate Bilirubin. This yellowish pigment causes yellowing of the person's eyes, skin and other tissues. Presenting a man with a case of retrovirus infection with complaints of abdominal distention, breathing difficulty and not able to have anything orally. He was started on liposomal Amphotericin B 250mg in 500ml of 5% dextrose over 4 hours infusion 1-0-0 for the treatment of fungal infection. Following the medication intake he developed altered liver function test results. This case describes the patient experiencing increase in bilirubin levels after administering Amphotericin B.

**Keywords:** Amphotericin B, Hyperbilirubinemia, Liver function tests, Antifungal management.

### INTRODUCTION

Liposomal Amphotericin B is active on relevant molds, yeasts which includes *Candida* spp., *Aspergillus* spp. is approved for the management of fungal infections. The dose of Liposomal Amphotericin B is 5 mg/kg/day. Management is for 1-2 weeks.<sup>1</sup> The side effects are fever and chills, headache, irregular heartbeat, nausea, vomiting and muscle cramps. Effects on the hepatic system have been rarely reported, including liver failure, hepatitis, and jaundice. Changes in liver function tests include increase in AST, ALT, GGT, bilirubin, and alkaline phosphatase. The most probable side effect of Amphotericin B is hyperbilirubinemia.<sup>2</sup> Adverse effects of liver is an important health issue in worldwide.<sup>3</sup>

In the management of many systemic fungal infections, Amphotericin B is the most effective agent, its use is complicated by serious adverse drug reactions. The main merit of the liposomal preparation is its lesser toxicity when taken by rapid intravenous injections.<sup>4</sup>

From the mid- 1950s, it is the most efficient antifungal drug for systemic mycoses and is the "gold standard" drug ever since 1960s.<sup>5</sup>

### CASE HISTORY

A 58 year old male patient is a known case of retroviral infection, on regular treatment with antiretroviral drugs with history of recurrent pleural effusion came to a tertiary care teaching hospital with complaints of abdominal distention, decreased sleep at night, fatigue, edema, abdominal pain, breathing difficulty, since 4 days. The breathing difficulty got aggravated on doing his routine activities. He was found to have hydropneumothorax on investigation and was started on

oxygen supplementation, steroids and antibiotics. On suspicion of TB he was started on anti-tubercular drugs. His initial lab results showed CRP: 81.5mg/l (<1mg/l), bilirubin (in urine): positive, haemoglobin: 8.2g/dl (13-17. g/dl), AST: 61.4 IU/L (5-35 IU/L), ALT: 46.6IU/L (5-45 IU/L), ALP: 307.3 (42-128 IU/L), Bilirubin total: 9.09mg/dl (0.2-1.2 mg/dl), Bilirubin direct: 4.56mg/dl (0-0.2 mg/dl). He was prescribed Amphotericin B 250mg in 500ml of 5% dextrose over 4 hours infusion 1-0-0 for the treatment of fungal infection. Five days after starting ATT, patient started developing elevation in liver enzymes and in view of this, ATT treatment was stopped. Liver enzymes started decreasing slowly but bilirubin levels were progressively increasing.

As Amphotericin B was included in therapy, the bilirubin levels started elevating: eg. Bilirubin total: 13.32 mg/dl on 6<sup>th</sup> day, 14.54mg/dl on 7<sup>th</sup> day, 14.18mg/dl on 8<sup>th</sup> day of drug therapy; Bilirubin direct: 6.39mg/dl on 6<sup>th</sup> day, 6.76mg/dl on 7<sup>th</sup> day, 6.59 on 8<sup>th</sup> day of drug therapy respectively. With the diagnosis of hyperbilirubinemia, Amphotericin B infusion was stopped. After stopping the drug his bilirubin levels dropped near to the normal level i.e Bilirubin total: 7.78mg/dl and bilirubin direct: 3.63mg/dl. Later on, it was seen that his bilirubin level was sliding to normal level.

### DISCUSSION

For the last 40 years Amphotericin B has been used to treat systemic fungal infections, aspergillosis and candidiasis. Hepatotoxicity related with Amphotericin B is rare.<sup>6</sup> Amphotericin B combines with ergosterol altering the membrane permeability in fungi, causing leak in the cell components with subsequent cell necrosis. Causes of pathologic hyperbilirubinemia can be classified as due to



elevated bilirubin load and or impaired bilirubin excretion.<sup>7</sup> Naranjo ADR probability scale was used for causality assessment with a score of 8 (probable). On managing this condition, the drug therapy was stopped on 29/10/16 (after a long period of 19 days drug infusion). The adverse effect warns to monitor bilirubin and LFT. The drug –induced hyperbilirubinemia shows a prevalence of 15-50% a year.<sup>8</sup> Affected individuals were managed with supplements of iron, blood transfusions and the offending agent was stopped.

## CONCLUSION

Antifungal drugs are the chief class of drugs causing hyperbilirubinemia. This state is partial, resulting in liver failure, which can show fatal results. Graduated pharmacist and registered medical representatives should have knowledge on this reaction so as to withdraw the offending substance or drug. Patient should also be educated regarding offending substance, to avoid future complications.<sup>9</sup>

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